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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,532	12/12/2001	Roberto Villa	9623 V/vmf/as	4029

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/009,532	VILLA ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response to Non-Final Office Action, the Amendment and Applicant's Arguments/Remarks, all filed 05/29/07 is acknowledged.

Claims 25-39 are pending in this action. Claim 25 has been amended. Claims 25-39 remain rejected.

Response to Amendment – New Matter

In the amendment filed 05/29/07, Applicants have amended independent claim 25 by incorporating the claim limitation that "said controlled release composition is in a solid form". This amendment introduces new matter into the claims. The Examiner fails to find support in the instant specification or the originally disclosed claims for the claim limitation "a solid form" as now claimed. Applicant directs the Examiner to page 8, line 18 and Examples 1-14 of the instant specification for support of the amended claim language. While ample support is provided for the composition being in the form of "*tablets, capsules and/or minitablets*", Applicant has not provided ample support for the limitation of a "*solid form*" as now claimed.

* * * * *

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauer *et al.* (U.S. Patent No. 5,342,625).

The instant invention is drawn to a controlled release composition, comprising: a hydrophilic first matrix comprising a lipophilic phase and an amphiphilic phase, wherein said lipophilic phase and said amphiphilic phase are in a second matrix together, and said second matrix is dispersed throughout the hydrophilic first matrix, wherein said lipophilic phase comprises lipophilic compounds and an active ingredient at least partially incorporated in said lipophilic phase and wherein said amphiphilic phase comprises an active ingredient at least partially incorporated in said amphiphilic phase, and wherein said controlled release composition is in a solid form.

Hauer *et al.* ('625) teach pharmaceutical compositions comprising cyclosporins as the active ingredient in microemulsion pre-concentrate and microemulsion form (see Abstract); (col. 1, lines 5-20). In addition to the cyclosporine active ingredient, the microemulsion pre-concentrate compositions will comprise: (1) a hydrophilic phase, (2) a lipophilic phase; and (3) a surfactant. The cyclosporine is carried in the lipophilic phase. Suitably both the hydrophilic and lipophilic phases will serve as carrier medium (col. 6, lines 35-53).

Especially preferred in accordance with the present invention are compositions as defined under (A) in which the hydrophilic phase comprises components, particularly TRANSCUTOL,

COLYCOFUROL and/or 1,2-propylene glycol (col. 7, line 19 – col. 8, line 42). TRANSCUTOL will generally be present in an amount of from about 1 to about 90% by weight (col. 17, lines 4-13).

Compositions defined under (A) additionally comprise a lipophilic phase (2) (col. 8, lines 56-57). Suitable components for use as lipophilic phase components include fatty acid triglycerides, neutral oils, e.g., neutral plant oils, in particular coconut oils commercially available under the trade name MIGLYOL (col. 8, line 58 – col. 9, line 20).

The compositions further comprise a surfactant component, which may comprise hydrophilic or lipophilic surfactants or mixtures thereof. Suitable surfactants disclosed include reaction products of natural or hydrogenated vegetable oils and ethylene glycol, i.e., polyoxyethylene glycolated natural or hydrogenated vegetable oils. Also disclosed are polyoxyethylene-sorbitan-fatty acid esters (col. 9, line 40 – col. 10, line 53).

Phospholipids, in particular lecithins are also suitable for use in the compositions of the invention (col. 10, lines 56-58).

Propylene glycol mono- and di-fatty acid esters such as propylene glycol dicaprylate and the like are also disclosed (col. 10, lines 60-65).

Celluloses and cellulose derivatives are disclosed at col. 12, line 65 – col. 13, line 12 and include hydroxyalkyl celluloses.

Additional suitable components taught include solid hydrocarbons, and vegetable and synthetic waxes provided in amounts of up to about 80% by weight (col. 23, lines 19-38).

The compositions may be employed orally in unit dosage forms, for example hard or soft gelatin capsules (col. 16, lines 25-41).

The compositions can comprise one or more carriers, or diluents, thickening agents, emulsifying agents and so forth (col. 22, lines 37-41).

Given the teachings of Hauer *et al.* discussed above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 25-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cottens *et al.* (WO 96/13273).

The instant invention is drawn to a controlled release composition, comprising: a hydrophilic first matrix comprising a lipophilic phase and an amphiphilic phase, wherein said lipophilic phase and said amphiphilic phase are in a second matrix together, and said second matrix is dispersed throughout the hydrophilic first matrix, wherein said lipophilic phase comprises lipophilic compounds and an active ingredient at least partially incorporated in said lipophilic phase and wherein said amphiphilic phase comprises an active ingredient at least partially incorporated in said amphiphilic phase and wherein said controlled release composition is in a solid form.

Cottens *et al.* ('273) teach pharmaceutical compositions comprising a microemulsion pre-concentrate comprising a difficultly soluble active agent and a carrier medium comprising: (1) a hydrophilic phase which comprises dimethylisosorbide and/or a lower alkyl alkanoic ester; (2) a lipophilic phase and (3) a surfactant. The active agent may be cyclosporine or a macrolide (see Abstract); (p. 2, lines 13-18); (p. 3, lines 22-24).

The composition may be in the form of a microemulsion, which additionally contains an aqueous phase, preferably water (p. 2, lines 20-23).

The lipophilic phase may comprise 5 to 85% by weight of the carrier medium (p. 3, lines 10-12). The hydrophilic phase may comprise 5 to 50% by weight of the carrier medium (p. 3, lines 17-18). The surfactant phase may comprise 5 to 80% by weight of the carrier medium (p. 3, lines 13-15).

The hydrophilic phase may also comprise a co-component selected from Transcutol. The hydrophilic co-components may also include ethanol (p. 6, lines 22-26).

The compositions can be in gelatin, encapsulated forms (p. 7, line 1), (p. 17, lines 25-26).

Preferred lipophilic phase components are medium chain fatty acid triglycerides, mixed mono-, di-, tri-glycerides and transesterified ethoxylated vegetable oils (p. 7, line 18 – p. 10, line 11).

Examples of suitable surfactants are listed at page 10, line 13 – p. 12, line 15. Phospholipids, in particular lecithins, are also disclosed (p. 12, lines 6-7).

Given the teachings of Cottens *et al.* discussed above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 05/29/07 have been fully considered but they are not persuasive.

- **35 U.S.C. 103(a) Rejection over Hauer et al. (US 5,342,625):**

Applicant argued, "HAUER discloses a galenic system capable of forming microemulsions spontaneously on contact with water alone (see column 6, lines 25-30). The HAUER composition is defined as a micro-emulsion preconcentrate formulation. While the examples reported in HAUER describe preparations in a liquid form, these liquid preparations are used to fill compositions such as gelatin capsules (see Example 7). Therefore, the compositions described in HAUER remain liquid compositions."

Applicant's arguments have been fully considered, but were not persuasive. Admittedly, while Hauer teach microemulsion formulations, the formulations of Hauer, as also noted by Applicant, can be used to fill capsules, such as gelatin capsules, which are solid forms. It is noted that Applicants themselves claim that their composition can be in the form of tablets or *capsules* (see for instance, instant claims 33-34). Thus, the microemulsion formulations taught by Hauer, which can be filled into capsules would be sufficient to meet the claims of the instant invention and would be suitable for their intended purpose, since the prior art recognizes that the formulations can be filled into solid dosage forms (i.e., capsules).

- **35 U.S.C. 103(a) Rejection over Cottens et al. (WO 96/13273):**

Applicant argued, "COTTENS discloses micro-emulsion preconcentrate preparations and define the preparation as follows: "...a composition which spontaneously form a microemulsion in an aqueous medium as water or gastric juice. The examples in COTTENS describe preparations in liquid form, which are used to fill gelatin capsules or used as drink solutions. Hence, the COTTENS' formulations are liquid."

Applicant's arguments have been fully considered, but were not persuasive. Cottens, as pointed out by Applicant, teach microemulsion preconcentrate formulations. While the preparations themselves are in liquid forms, Cottens teaches that the preparations can be filled into capsules, such as gelatin capsules, which are solid forms. It is noted that Applicants themselves claim that their composition can be in the form of tablets or *capsules* (see for instance, instant claims 33-34). Thus, the microemulsion preconcentrate formulations taught by

Cottens, which can be filled into capsules would be sufficient to meet the claims of the instant invention and would be suitable for their intended purpose, since the prior art recognizes that the formulations can be filled into solid dosage forms (i.e., capsules).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

- No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

August 20, 2007

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